

REMARKS

This amendment under 37 C.F.R. § 1.111 is being submitted in response to the outstanding Official Action mailed April 2, 2003. In view of the above claim amendments and the following remarks, reconsideration and allowance of this application is respectfully requested.

Claims 1 and 10 have been amended to more particularly point out and distinctly claim the subject matter that applicant regards as the invention. In particular, both claims have been amended to incorporate the subject matter of claim 20 defining the polymerizable functional groups as -OH and dicarboxylic acid groups. Claims 21 and 23 have been amended to conform with the changes to claim 10. Because the subject matter was presented in original claim 20, the claim amendments do not introduce new matter.

Claims 1 and 10 have also been amended to clarify that the first and second monomer series each has a single homologous variation. This is shown in the polyarylate library in the Examples and also does not introduce new matter. Finally, Claims 1 and 10 have been amended to require that the number of copolymers as well as the polymer molecular weight and polydispersity be selected to provide meaningful library-wide incremental structure-property correlations. This is disclosed in the specification at page 3, lines 23-27, page 11, lines 9-13 and page 13, lines 14-23 and also does not introduce new matter. Implicit within the cited portions of the specification (to one of ordinary skill in the art) is that for correlations to be "meaningful" the data produced thereby must be statistically significant. This is reflected in the Examples presented in the specification, as are the "library-wide" structure-property correlations.

In view of these amendments the claims are believed to be in condition for allowance. Reconsideration of the rejections made by the Examiner is therefore respectfully requested.

Turning to the Official Action, claims 1-3, 5, 9, 10, 14, 17, 18, 20, 21, 23, 24, 26 and 27 were rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter applicants regard as the invention. Two separate indefiniteness rejections are made.

First, the term the term "number of homologously bivariant copolymers sufficient to incrementally establish quantitative structure-property correlations" was considered indefinite. According to the Examiner, the number of polymers would be variable from one type of polymer to another and variable depending upon what quantitative structural property is being evaluated. The Examiner also considered this a relative term rendering the claims indefinite in the absence of a definition in the claims or a standard disclosed in the specification for ascertaining the requisite degree necessary to meet this limitation and reasonably apprise one of ordinary skill in the art of the scope of the invention..

Next, the Examiner considered the terms "selected to have comparable reactivities" and "of sufficiently high molecular weight and similar polydispersity" to be relative terms that render the claims indefinite. According to the Examiner, the absence of a definition in the specification for ascertaining the requisite molecular weight and polydispersity prevented one of ordinary skill in the art from being reasonably apprised of the scope of the invention.

These rejections are respectfully traversed in view of the above claim amendments for the reasons set forth hereinafter.

Claims 2, 3, 18 and 20 have been canceled. Claims 1 and 10 have been amended so that they are now directed to copolymers with -O-C(=O)- linkages formed by reacting monomers having polymerizable -OH groups with monomers having polymerizable carboxylic acid groups. Claims 5, 9, 14, 17, 21, 23, 24, 26 and 27 incorporate this limitation by being directly or indirectly dependent from claims 1 and/or 10. In this context the meaning of the terms objected to by the Examiner as the basis for his rejections become sufficiently clear to satisfy the requirements of 35 U.S.C. §112, second paragraph.

In particular, the claims as amended now define copolymers with -O-C(=O)- ester-type linkages. Whether or not the number of polymers needed to incrementally establish library-wide quantitative structure-property correlations varies with the type of polymer is now irrelevant.

Requiring the number of polymers to be sufficient to incrementally establish library-wide quantitative structure-polymer correlations serves to define the claimed copolymer library over collections of polymers useless for this purpose because the number of polymers in the collection are insufficient provide relevant data to achieve this goal.

One of ordinary skill in the art who is informed by the present specification that the goal is to establish library-wide structure-property correlations among polymers of two monomer series, each having a single homologous variation, and who then selects a structure-

property correlation of interest, can readily determine not only how many polymers are needed, but also the proper distribution of polymers within the array for relevant data to be obtained.

Thus, defining the number of polymers within the library as an amount sufficient to produce meaningful library-wide incremental structure-property correlations is not relative to the point of indefiniteness to one having ordinary skill in the art. Rather, it is a matter of common sense. As reflected in the Examples, and as understood by one of ordinary skill, “meaningful” correlations refers to the generation of data that is statistically relevant. One of ordinary skill in the art would know when looking at a given polymer library whether a sufficient number of polymers and were properly distributed within a library to generate statistically significant incremental structure-property correlations over the entire library.

~~This is particularly true for the class of polymers to which claims 1 and 10 are now directed.~~ By amending claims 1 and 10 to limit the subject matter to polymers with -O-C(=O)- linkages, and to clarify that the number of polymers must be sufficient to produce meaningful library-wide correlations, the term “number of homologically bivalent polymers sufficient to establish meaningful structure-property correlations” is unambiguous. By amending claims 1 and 10 in this manner, this portion of the rejection under 35 U.S.C. §112, second paragraph has thus been overcome. Reconsideration by the Examiner and withdrawal of the rejection in therefore respectfully requested.

Regarding the terms “comparable reactivities” and “of sufficiently high molecular weight and similar polydispersity,” claims 1 and 10 have been amended to better define the

meaning of these terms within the claims in the context of the standards described in the specification. In particular, the claims now require the use of monomers of comparable reactivity to permit the same polymerization conditions to be used in a way that results in polymers of sufficiently similar molecular weights and polydispersities to establish meaningful library-wide structure-property correlations.

The specification explains at page 10, lines 24-28 that the purpose of using monomers of roughly identical reactivity was to ensure that all polymers within the library, when prepared under identical reaction conditions, reach comparable, i.e., statistically significant, molecular weights. At page 11, lines 9-11, the specification discloses that sufficiently similar molecular weights and polydispersities allow meaningful, i.e., statistically relevant, comparison of material properties between polymers. That is, the molecular weights and polydispersities should be sufficiently similar among the polymers to permit statistically relevant comparisons of polymer properties to be made over the entire library.

So guided by the specification, one having ordinary skill in the art would know how to select monomers with sufficiently similar reactivities to produce polymers with molecular weights and polydispersities sufficiently similar to permit a relevant comparison of polymer properties across the entire library. This is also particularly true for the class of polymers to which claims 1 and 10 are now directed. By being limited to polymers with -O-C(=O)- linkages, and clarifying that the degree to which monomer reactivity must be similar is that which produces molecular weights and polydispersities sufficiently similar to make meaningful comparisons of polymer properties across the entire library, the meaning of the claim terms objected to by the examiner is now unambiguous. By amending claim 1 and 10

in this manner, this portion of the rejection under 35 U.S.C. §112, second paragraph has thus been over come. Reconsideration by the Examiner and withdrawal of the rejection is therefore respectfully requested.

Next, claims 1-3, 5, 9, 10, 14, 17, 18, 20, 21, 23, 24, 26 and 27 were rejected under 35 U.S.C. §112, first paragraph for new matter as containing subject matter which was not described in the specification as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of the claimed invention. The Examiner considered the limitations added to the claims by the Amendment dated January 10, 2003 to contain new matter to the extent that the claims were broadly applicable to copolymer libraries other than the polyarylates of tyrosine derived diphenols and diacids disclosed at pages 10-11 of the specification. This rejection is respectfully traversed for the reasons set forth hereinafter.

Claims 2, 3, 18 and 20 have been canceled. Claims 1 and 10 have been amended so that they are now directed to copolymers with -O-C(=O)- linkages formed by reacting monomers having polymerizable -OH groups with monomers having polymerizable carboxylic acid groups. The use of such monomers to form such polymers is supported by original claim 20. Support for the other limitations previously added was identified in the January 10, 2003 amendment.

The specification as filed thus reasonably conveyed to one skilled in the art that the inventors at the time the application was filed had possession of this invention defined by claims 1 and 10 as amended. By amending claims 1 and 10 in this manner, this rejection

under 35 U.S.C. §112, first paragraph has thus been overcome. Reconsideration by the Examiner and withdrawal of the rejection is therefore respectfully requested.

Next, claims 1-3, 5, 9, 10, 14, 17, 18, 20, 21, 23, 24, 26 and 27 were rejected under 35 U.S.C. §112, first paragraph for lack of written description as containing subject matter which was not described in the specification as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of the claimed invention. The Examiner considered the copolymers claimed to lack metes and bounds because each of the individual monomers is varied as to monomer core structure in a completely open ended manner incorporating one or more variations therein, and the polymer libraries can be modified by chemical reaction or cross-linking without indication as to what types of chemical reactions or cross-linking is encompassed.

~~The Examiner also considered the specification to lack guidance for designing core~~
monomer structures that will predictably result in potentially useful library compounds beyond vague assertions that one needed to obtain a library of polymers where selected end-use properties change in a predictable and systemic fashion. This rejection is respectfully traversed in view of the above claim amendments for the reasons set forth hereinafter.

Claims 2, 3, 18 and 20 have been canceled. Claims 1 and 10 have been amended so that they are now directed to copolymers with -O-C(=O)- linkages formed by reacting monomers having polymerizable -OH groups with monomers having polymerizable carboxylic acid groups. Claims 1 and 10 have also been amended to clarify that each monomer series has but one homologous variation.

Claims 1 and 10 are thus no longer open ended with respect to the type of polymer or the number of homologous variations within the monomer series from which the polymers are polymerized, so that the scope of the claimed copolymer no longer lacks metes and bounds. Furthermore, the scope of the claims have been limited so that the examples are now fairly representative of the claimed copolymer species and represent a substantial portion of the claimed genus. The specification as filed thus reasonably conveyed to one skilled in the art that the inventors at the time the application was filed had possession of this invention defined by claims 1 and 10 as amended.

Regarding claims 9 and 27, and the types of "chemical reactions" and/or "cross-linking" encompassed by these claims, it is implicit from the level of disclosure provided in the specification that applicants only intended these reactions to be those already conventional to the art. For example, cross-linking reactions are ubiquitous, the further modification of biocompatible polymers via covalent attachment of biological or pharmaceutically active moieties is also well-known. With the scope of the claimed subject matter now limited to copolymers with -O-C(=O)- linkages formed by reacting monomers having polymerizable -OH groups with monomers having polymerizable carboxylic acid groups, the types of further modifications that can be employed have been significantly limited and are readily identified by those familiar with the core co-polymerization process, so that the specification as filed thus reasonably conveyed to one skilled in the art that the inventors at the time the application was filed had possession of this invention defined by claims 9 and 27.

The amendments to claims 1 and 10 have thus overcome the written description rejection under 35 U.S.C. §112, first paragraph. Reconsideration by the Examiner and withdrawal of the rejection is therefore respectfully requested.

Next, claims 1-3, 5, 9, 10, 14, 17, 18, 20, 21, 23, 24, 26 and 27 were rejected under 35 U.S.C. §112, first paragraph for lack of enablement, because the specification was only enabling for a copolymer array of "polyacrylate" copolymers prepared by the condensation of tyrosine derived diphenol compounds and dicarboxylic acids and does not enable any person skilled in the art to make and use the invention commensurate in scope with the claims. This rejection is respectfully traversed in view of the above claim amendments for the reasons set forth hereinafter.

Presumably, the Examiner is referring to polyarylates. Claims 1 and 10 have been amended so that they are now directed to copolymers with -O-C(=O)- linkages formed by reacting monomers having polymerizable -OH groups with monomers having polymerizable carboxylic acid groups. Claims 1 and 10 have also been amended to clarify that each monomer series has but one homologous variation. Claims 2, 3, 18 and 20 have been canceled.

The claims are now clearly limited to polymer species for which there clearly exists adequate guidance in the specification for making and using the polymer libraries claimed in the context of what one skilled in the art already knows regarding the preparation of the polymers claimed. The amendments to claims 1 and 10 have thus overcome the enablement rejection under 35 U.S.C. §112, first paragraph. Reconsideration by the Examiner and withdrawal of the rejection is therefore respectfully requested.

Next, claims 1-3, 5, 9, 10, 14, 17, 18, 20, 21, 23, 24, 26 and 27 were rejected under 35 U.S.C. §102(a) as being anticipated by, or in the alternative for being obvious over (presumably under 35 U.S.C. §103(a)) over Brocchini et al. JACS Vol. 119 (5/19/97) pages 4553-4554. Brocchini et al. was cited as teaching a library of 112 homologously bivariant polyarylates, which the Examiner considered sufficient to incrementally establish quantitative structure property correlations, and which the Examiner otherwise considered to meet each and every limitation of the claims. This rejection is respectfully traversed for the reasons set forth hereinafter.

The authors of Brocchini et al. are the inventors of the present application. Brocchini et al. is therefore not properly prior art under 35 U.S.C. §102(a) because it does not represent knowledge or use "by another" before the invention of the claimed subject matter by the inventors. Reconsideration by the Examiner and withdrawal of this rejection is therefore respectfully requested.

Next, claims 1-3, 5, 9, 10, 14, 17, 18, 20, 21, 23, 24, 26 and 27 were rejected under 35 U.S.C. §102(b) as being anticipated by, or in the alternative for being obvious over (again presumably under 35 U.S.C. §103(a)) over Fiordeliso et al., alone, or if necessary, further in view of Brocchini et al. Fiordeliso et al. was cited as teaching a library of five distinct polyarylate copolymers prepared from tyrosine-derived diphenols and dicarboxylic acids and suggesting the synthesis of larger libraries from seven different diphenols and seven different dicarboxylic acids. This rejection is respectfully traversed in view of the above claim amendments for the reasons set forth hereinafter.

As noted above, Brocchini et al. is not prior art against the presently claimed invention. This is a classic example of the impermissible application of hindsight reconstruction to use what was learned from the inventor's own teachings to either directly or subliminally supply what is missing in the disclosure of Fiordeliso et al. to conclude that the claims are obvious. Viewed alone, Fiordeliso et al. does not teach or suggest the instant invention as it is presently claimed. The present invention represents an extension by the inventors of the work disclosed by Fiordeliso et al.

The present inventors discovered that the monomers within each monomer series have to be selected to have comparable reactivities to permit the same polymerization conditions to be employed for each parallel synthesis reaction so that the polymers all have sufficiently similar molecular weights and polydispersities to establish relevant structure-property correlations that are valid over the entire library. The five polyarylates reported by Fiordeliso et al. ~~are not a sufficient number to permit meaningful library-wide structure-property correlations~~ to be made. Any suggestion by Fiordeliso et al. to expand the library does not take into consideration how to control the reaction conditions to ensure an *expanded* library of polymers are prepared that are sufficiently similar to permit relevant structure-property comparisons over *the entire library*. To the extent that any of the necessary steps are mentioned as possible reaction conditions, there is no recognition that such conditions are required for library expansion, so that the present invention represents an invention of selection over whatever elements of the invention can be gleaned from Fiordeliso et al.

The amendments to claims 1 and 10 that require the library to consist of polymers between which meaningful structure-property correlations can be drawn refines the distinc-

tion between the subject matter claimed and the Fiordeliso et al. disclosure. By amending claims 1 and 10 in this manner, this rejection under 35 U.S.C. §102(b) as being anticipated by, or in the alternative for being obvious under 35 U.S.C. §103(a), over Fiordeliso et al. has thus been overcome. Reconsideration by the Examiner and withdrawal of this rejection is therefore respectfully requested.

Next, claims 1-3, 5, 9, 10, 14, 17, 18, 20, 21, 23, 24, 26 and 27 were rejected under 35 U.S.C. §102(b) as being anticipated by, or in the alternative for being obvious over (again presumably under 35 U.S.C. §103(a)) Kohn et al., U.S. Patent No. 5,216,115. Kohn et al. was cited as teaching a library of five distinct polyarylate copolymers prepared from tyrosine-derived diphenols and dicarboxylic acids and inherently disclosing libraries of polymers of sufficiently high molecular weights and similar polydispersities that would incrementally establish quantitative structure-property correlations. The Examples were cited as disclosing the screening of a library for structure-property correlations. This rejection is respectfully traversed in view of the above claim amendments for the reasons set forth hereinafter.

Kohn et al. issued from the patent application directed the work disclosed by the Fiordeliso et al. journal article and not only fails to anticipate the presently claimed invention, it teaches even less that Fiordeliso et al. Structure-property correlations are only given for three to five polymers, which reveals nothing of relevance for the polymer family and is uninformative for what can be expected library-wide for larger polymer arrays.

Like Fiordeliso et al., any suggestion to expand the library does not take into consideration how to control the reaction conditions to ensure an expanded library of

polymers are prepared that are sufficiently similar to permit relevant library-wide structure-property comparisons. To the extent that any of the necessary steps are mentioned as possible reaction conditions, there is no recognition that such conditions are required for library expansion, so that the present invention represents an invention of selection over whatever elements of the invention can be gleaned from Kohn et al.

The amendments to claims 1 and 10 that require the library to consist of polymers between which meaningful library-wide structure-property correlations can be drawn therefore also patentably distinguishes over Kohn et al. under both 35 U.S.C. §§102(a) and 103(a). By amending claims 1 and 10 in this manner, this rejection under 35 U.S.C. §102(b) as being anticipated by, or alternatively for being obvious under 35 U.S.C. §103(a), over Kohn et al. has thus been overcome. Reconsideration by the Examiner and withdrawal of this rejection is therefore respectfully requested.

Finally, the Examiner maintained the rejections of claims 1-3, 5, 9, 10, 14, 17, 18, 20, 21, 23, 24, 26 and 27 for being obvious under 35 U.S.C. §103(a) over Kohn et al., U.S. Patent No. 5,216,115, the Gordon et al. J. Med. Chem. journal article, and Still et al., U.S. Patent No. 5,565,324, and also for being obvious over Kohn et al., U.S. Patent No. 4,980,449, Gordon et al. and Still et al., essentially for reasons of record. The Examiner also refuted Applicant's remarks that were submitted to distinguish the cited prior art combinations, including observations that the presently claimed libraries could be produced by a single pot process and that the presently claimed libraries encompassed oligomers as disclosed by Still et al. This rejection is respectfully traversed in view of the above claim amendments for the reasons set forth hereinafter.

As recognized by one of ordinary skill in the polymer art, the presently claimed copolymer libraries do not encompass oligomers because the structural properties of oligomers do not resemble the structural properties of corresponding polymers. The terms are not interchangeable. No meaningful correlations to polymer structural properties for the library as a whole can be gleaned from oligomer data.

One of ordinary skill in the polymer art also recognizes that the presently claimed library of polymers with similar molecular weights and polydispersities cannot be made in a single pot process. This results in an inseparable mixture from which individual polymer species cannot be separated for the determination of structure-property correlations.

In any event, neither combination of prior art teaches or suggest how to control the reaction conditions to ensure an expanded library of polymers are prepared that are sufficiently similar to permit relevant library-wide structure-property comparisons. The Kohn et al. patents depict properties for a limited number of polymer structures. Gordon et al. and Still et al. do not teach or suggest the conditions necessary for a library of *polymers* to be produced within which relevant library-wide structure-property correlations can be made.

The amendments to claims 1 and 10 that require the library to consist of polymers between which meaningful library-wide structure-property correlations can be drawn therefore also patentably distinguishes over both cited prior art combinations under 35 U.S.C. §103(a). By amending claims 1 and 10 in this manner, both rejections for being obvious under 35 U.S.C. §103(a), over the cited prior art combinations have thus been overcome.

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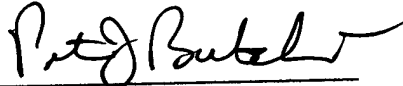
Reconsideration by the Examiner and withdrawal of this rejection is therefore respectfully requested.

In view of the above claim amendments and the foregoing remarks, this application is now in condition for Allowance. Reconsideration is respectfully requested. The Examiner is requested to telephone the undersigned if there are any remaining issues in this application to be resolved.

Finally, if there are any additional charges in connection with this response, the Examiner is authorized to charge applicants' Deposit Account No. 19-5425 therefor.

Dated: October 2, 2003

Respectfully submitted,



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